

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : A61K 7/48	A1	(11) International Publication Number: WO 94/10970 (43) International Publication Date: 26 May 1994 (26.05.94)
(21) International Application Number: PCT/EP93/02883 (22) International Filing Date: 19 October 1993 (19.10.93) (30) Priority data: 92310222.2 9 November 1992 (09.11.92) EP (34) Countries for which the regional or international application was filed: GB et al. (71) Applicant (for all designated States except US): QUEST INTERNATIONAL B.V. [NL/NL]; Huizerstraatweg 28, NL-1411 GP Naarden (NL). (72) Inventors; and (75) Inventors/Applicants (for US only) : CHEETHAM, Peter, Samuel, James [GB/GB]; 28 Meadway, Harrold, Bedford, MK43 7DR (GB). GRAAF, Thalie, Paulina [NL/GB]; 63 Greenhields, Bedford, MK40 3TU (GB). JAN-OUSEK, Angela [GB/GB]; Juniper House, 5A Woodlands Way, Off Giles Lane, Canterbury CT2 7LS (GB). KLEIN, Erich [AT/AT]; Purgstall 167, A-8063 Eggersdorf (AT). WATKINS, Stephen, David [GB/GB]; 7 Kiln Close, Challock, Nr Ashford, Kent TN25 4DA (GB).		(74) Agent: DEKKER, Enno, E., J.; Unilever N.V., Patent Division, P.O. Box 137, NL-3130 AC VLAARDINGEN (NL). (81) Designated States: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: SOLUBILIZING AGENTS (57) Abstract The invention relates to the use of monoalkyl citrates having an alkyl group of 7-10 carbon atoms as solubilizing agents in perfumery, cosmetics, personal care and household products consisting of oil-in-water emulsions as well as to hydrophobic cosmetic, personal care and household product ingredients containing such monoalkyl citrates. The emulsions preferably contain at least 0.01 % w/w of monoalkyl citrate. Especially preferred is mono-octyl citrate.		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

Solubilizing agents

The invention relates to the use of monoalkyl citrates as solubilizing agents in perfumery, cosmetics, personal care and household products. The invention particularly relates to cosmetic, personal care and household products consisting of oil-in-water emulsions as well as to hydrophobic cosmetic, personal care and household product ingredients containing such monoalkyl citrates.

10

Various citric acid esters have been known for different uses in cosmetic preparations.

Thus, in EP 006234, EP 006232, and US 4,010,253 the use of citric acid esters of 1-6C alcohols as deodorants in various cosmetic products is described. It is stressed that the trialkyl esters are highly preferred for this purpose. It is also stressed that the cosmetic product should have a low water content, preferably below 5% w/w, unless the citric acid ester is used in conjunction with an antioxidant.

20

In DE 2361716 the use of mixed esters, obtained by complete esterification of citric acid with a mixture of aliphatic diols and 12-30C aliphatic monoalcohols, as water-in-oil emulsifiers is described. The products are suitable for skin creams and the like.

25

Certain long-chain 2-hydroxyalkylesters of citric acid, obtained by reacting terminal long-chain epoxides with citric acid have been found to be water-in-oil emulsifiers (P. Lorenz et al, 10th IFSCC Congress, Cosmetic Horizons, Sydney, Australia, 25-27th October 1978, Vol 2.).

30

In EP 199131 derivatives, such as alkali or alkaline earth metal salts, of mono-, di-, or tri-esters of citric acid and polyoxy(2-4C)alkylated

mono-(8-20C)-alcohols have been described as emulsifiers which are useful for e.g. cosmetics.

GB 1,448,792 describes mono- and di-esters prepared from citric acid and 12-22C alkyl lactates and their use as emulsifiers in e.g. cosmetics.

In EP 282289 skin-smoothing compositions are disclosed containing salts of monoesters of citric acid and 10-18C alcohols and (poly)ethoxylated alcohols.

Monoesters of citric acid are also employed in the food technology art. U.S. Patent No. 2,158,678 (Gooding et al.) describes agents said to retard the development of rancidity and improve moisture retention in glyceridic oil compositions, e.g., margarine. These agents, defined at col. 1, line 45 to col. 2, line 25, include mono-

lauryl citrate and monostearyl citrate. Related U.S. Patent No. 2,523,792 (Vahlteich et al.) describes edible compositions which are said to retard rancidity in glyceridic oils and which have 15 to 37.5% of selected monoesters of citric acid (including monolauryl, mono-myristyl, monopalmityl, monooleyl and monostearyl citrate) dissolved in a solubilizing agent, e.g.

lecithin. Monoesters of citric acid are also said to retard deterioration of milk and egg products in U.S. Patent 2,667,419 (Gooding et al.). Citric acid

monoesters of decanols, dodecanols, hexadecanols, and octadecanols are particularly disclosed and more particularly monolauryl and monostearyl citrate. Also, U.S. Patent No. 2,902,372 (Harris) discloses monoesters of citric acid with aliphatic alcohols of less than 3 carbon atoms for the purpose of improving the whipping properties of egg whites. Finally, U.S. Patent No.

3,004,853 (Julian et al.) discloses citric acid esterified with cetyl alcohol as part of an emulsifier system in a liquid shortening.

In the perfumery, cosmetics, personal care and household products industry there is a need for solubilizers which

can be used to prepare clear oil-in-water microemulsions of perfumes or other hydrophobic ingredients, which solubilizers are innocuous to the skin.

5 It has now been found that mono-alkyl citrates wherein the alkyl group has 7-10 carbon atoms are excellent solubilizers which may be used to provide stable oil-in-water emulsions of perfumes and other hydrophobic liquid ingredients of cosmetic, personal care and household
10 products. They are especially suitable to provide clear o/w microemulsions. To distinguish clear o/w microemulsions from o/w emulsions in general the former will hereinafter be referred to as "microemulsions". Perfumes and other hydrophobic liquid ingredients of cosmetic,
15 personal care and household products will hereinafter be referred to simply as "hydrophobic liquids"

The monoalkyl citrates are completely innocuous, even to delicate skins. Contrary to what might have been derived
20 from the prior art, they are stable in aqueous media also in the absence of antioxidants. Finally they are completely miscible with most perfume components and other hydrophobic liquids and can therefore be used as diluents for perfumes and other hydrophobic liquids,
25 especially if these are intended to be used in emulsion, particularly in microemulsions.

The invention therefore provides cosmetic, personal care and household products consisting of emulsions
30 comprising an aqueous phase, at least one hydrophobic liquid and a 7-10C monoalkyl citrate. Furthermore, the invention provides mixtures of one or more hydrophobic liquids and 7-10C monoalkyl citrates.

35 The presence of already relatively small quantities of monoalkyl citrates in hydrophobic liquids gives rise to a clearly noticeable improvement of emulsion stability

and ease of emulsification when such ingredients are incorporated in an emulsion type cosmetic or personal care or household product. For microemulsions an improvement of clarity is obtained. Thus, mixtures of hydrophobic liquids and a monoalkyl citrate usefully contain 0.5% w/w or more of the monoalkyl citrate, preferably at least 2% w/w and more preferably at least 5% w/w. On the other hand, such mixtures may comprise up to 95% w/w, preferably up to 90% w/w of the monoalkyl citrate. The monoalkyl citrates are especially useful for solubilizing perfumes and therefore the hydrophobic liquids part in the mixtures mentioned above may consist for a large part (e.g. 50% w/w or more) or even completely of perfume. Other hydrophobic liquids which may be solubilized by the monoalkyl citrates, and therefore be present in relatively large quantities in the hydrophobic liquid mixture, are skin emollients such as isopropyl myristate.

The quantity of monoalkyl citrate to be incorporated in a cosmetic, personal care or household product according to the invention depends on the quantity of hydrophobic liquid to be emulsified and for microemulsions on the desired degree of clarity. Generally the emulsions/microemulsions should contain at least 0.01% w/w, preferably at least 0.1%, more preferably at least 1% w/w of the monoalkyl citrate, whereas a quantity of more than 30% w/w will usually not be required. The preferred monoalkyl citrate for the purposes of the invention is monooctyl citrate.

For the purposes of this invention "cosmetic products" are products intended for increasing the appeal, visually or olfactively, of the human body. Likewise "personal care products" are products intended for cleaning, smoothening or otherwise improve the health and well-being of the outside of the human body. These

definitions of cosmetic and personal care products at least partially overlap since many products provide functions in both categories. Examples of such products in microemulsion form are: perfumes and like products known as "eau de toilette" and "eau de parfum", hand and body lotions, skin tonics, shaving products, bath and shower products, deodorant and antiperspirant products, hair care products such as shampoos and hair conditioners, mouth and dental care products. Such products are well known in the art. Thus, examples of skin care products are described in "Harry's Cosmeticology", R.G. Harry, 6th edition, Leonard Hill Books (1973), Chapters 5-13, 18 and 35; examples of deodorants and antiperspirants are described in C. Fox, Cosmetics and Toiletries 100 (Dec. 1985), pp 27-41; examples of hair care products are described in "Harry's Cosmeticology", vide supra, chapters 25-27; examples of dental care products are described in M. Pader, Oral Hygiene: Products and Practice, Marcel Dekker, New York (1988). Cosmetic and personal care products are usually perfumed, on the one hand to give a pleasant odour to the products themselves and on the other hand to have de body parts to which they are applied emit a pleasant odour after their use.

25

For the purposes of this invention "household products" are products intended for: laundry and textiles care such as washing, bleaching, softening and ironing; cleaning, disinfecting, scouring, polishing or shining hard surfaces, air treatment such as room deodorizing and air freshening

30

The emulsions generally also contain various components which are usually present in cosmetic, personal care or household products and which comprise, depending on the type of product, one or more of: various detergents or emulsifiers of the anionic, cationic, amphoteric or

35

nonionic type; bleaches; scouring powders; various organic solvents such as ethanol or isopropanol; humectants; viscosity modifiers; gelling agents; mineral or vegetable oils; waxes; colourants; pearlescent agents; preservatives; physiological coolants; etc.

The monoalkyl citrates according to the invention have been found to possess antimicrobial properties against various microorganisms which could cause microbiological spoilage in cosmetic, personal care and household products and thus the incorporation of a separate preservative may not be necessary in many cases, or the amount of preservative could be substantially lower than would be necessary without the presence of the monoalkyl citrate.

The monoalkyl citrates may be prepared according to various methods known in the art, e.g. as described in EP 282289.

As used herein, the term "perfume" denotes a substantially water-insoluble composition of matter consisting of one or more perfume components, optionally mixed with a suitable solvent or diluent, which is used to impart a desired odour to the cosmetic, personal care or household product to which it is added and/or to the skin or hair to which this product is applied. Perfume components are those constituents of a perfume which are added thereto only or primarily for their olfactive contribution. Perfume components may be natural such as essential oils, absolutes, resinoids, resins, concrètes, etc., and synthetic such as hydrocarbons, alcohols, aldehydes, ketones, ethers, acids, esters, acetals, ketals, nitriles, etc., including saturated and unsaturated compounds, aliphatic, carbocyclic and heterocyclic compounds.

The term "clear" as herein applied to microemulsions denotes a product which is transparent or translucent when observed through a layer of not more than 10cm thickness. Preferably the cosmetic and personal care products according to the invention have a turbidity of below 45 FTU, more preferably below 35 FTU. Turbidity is measured using a standard turbidity photometer and expressed in American Standard Farmaze Turbidity Units (FTU). The higher the value, the more turbid the solution.

The following examples are intended to illustrate the invention, However, the invention is not limited thereto.

15

Example 1

Two samples of the same perfume were made, one contained 10% w/w of the standard diluent diethyl phthalate whilst the other contained 10% w/w monoethyl citrate instead. Each perfume was added to a standard shampoo base and the turbidity measured using a turbidity photometer. The results are presented below.

		% w/w	% w/w
25	Shampoo base	99.7	99.7
	Perfume with monoethyl citrate	0.3	-
	Perfume with diethyl phthalate	-	0.3
	Total	100.0	100.0
30	Turbidity (in FTU)	24.0	42.0

Example 2

Two samples of the same low alcohol aftershave were made according to the recipes below, wherein one contained 3% w/w of monoethyl citrate whereas the other contained 3% w/w extra water. The turbidity of the aftershave was

35

measured using a turbidity photometer. The results are presented below.

		% w/w	% w/w
	Perfume	0.4	0.4
5	Ethanol	20.0	20.0
	Water	76.3	79.3
	Tris-aminomethane	0.3	0.3
	Monooctyl citrate	<u>3.0</u>	<u>-</u>
	Total	100.0	100.0
10	Turbidity	27.0	163.0

Example 3

Two samples of the same toner were made according to the recipes below, wherein one contained 3% w/w of monooctyl citrate whereas the other contained 3% w/w extra water. The turbidity of the toner was measured using a turbidity photometer. The results are presented below.

		% w/w	% w/w
20	Perfume	0.40	0.40
	Water	90.83	93.83
	Propylene glycol	5.00	5.00
	Tris-aminomethane	0.75	0.75
25	Red 33 (as 0.5% solution)	0.02	0.02
	Monooctyl citrate	<u>3.00</u>	<u>-</u>
	Total	100.00	100.00
	Turbidity	3.4	558.0

30

Example 4

Two samples of the same face mask were made according to the recipes below, wherein one contained 3% w/w of monooctyl citrate whereas the other contained 3% w/w extra water. The turbidity of the face mask was measured using a turbidity photometer. The results are presented below.

35

		% w/w	% w/w
	Perfume	0.5	0.5
	Polyvinylpyrrolidon	5.0	5.0
	Polyvinyl alcohol (10% aqueous soln.)	91.0	91.0
5	Water	-	3.0
	Tris-aminomethane	0.5	0.5
	Monooctyl citrate	<u>3.0</u>	<u>-</u>
	Total	100.0	100.0
10	Turbidity	32.0	516.0

CLAIMS

1. Cosmetic, personal care and household products
5 consisting of o/w emulsions comprising an aqueous phase,
a hydrophobic liquid and a monoalkyl citrate having an
alkyl group of 7-10 carbon atoms.
2. Cosmetic, personal care and household products
10 according to claim 1 wherein the quantity of monoalkyl
citrate is 0.01 - 30% w/w of the total emulsion.
3. Cosmetic, personal care and household products
15 according to claim 1 or 2 wherein the hydrophobic liquid
part consists for 50% w/w or more of perfume
4. Cosmetic, personal care and household products
20 according to any one of claims 1-3 wherein the emulsions
are clear microemulsion
5. Cosmetic, personal care and household products
according to claim 4 wherein the microemulsion has a
turbidity below 45 FTU.
- 25 6. Cosmetic, personal care and household products
according to any one of claims 1-5 wherein the monoalkyl
citrate is monoethyl citrate.
7. Mixtures consisting of one or more hydrophobic
30 liquids and a monoalkyl citrate having an alkyl group of
7-10 carbon atoms.
8. Mixtures according to claim 7 wherein the quantity
of monoalkyl citrate is 0.5 -95% by weight.

9. Mixtures according to any one of claims 7 and 8 wherein the hydrophobic liquid part consist for 50% w/w or more of perfume.

- 5 10. Mixtures according to any one claims 7-9 wherein the monoalkyl citrate is monooctyl citrate.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 93/02883

A. CLASSIFICATION OF SUBJECT MATTER

IPC 5 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 5 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US,A,5 049 699 (M.P. KOTOCK) 17 September 1991 see claims 1,2; examples 1,2 -----	1-10

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *A* document member of the same patent family

Date of the actual completion of the international search

25 February 1994

Date of mailing of the international search report

16. 03. 94

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+ 31-70) 340-3016

Authorized officer

Willekens, G

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internal Application No

PCT/EP 93/02883

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-5049699	17-09-91	NONE	

THIS PAGE BLANK (USPTO)